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THE ROLE OF HIGH-DOSE INTRAVENOUS METHYLPREDNISOLONE IN THE TREATMENT OF VARICELLA ASSOCIATED THROMBOCYTOPENIC PURPURA*

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SUMMARY: Aji DY, Altınkaya N, Güler A, Ayhan YI, Erginel A, Cenani A. (Department of Pediatrics, İstanbul University Faculty of Medicine at Cerrahpaşa, İstanbul, Turkey). The role of high-dose intravenous methylprednisolone in the treatment of varicella associated thrombocytopenic purpura. Turk J Pediatr 35: 69-73, 1993.

Two children with varicella associated thrombocytopenia are presented. Case 1, evidencing no mucosal or parenchymal bleeding was administered prednisone 2 mg/kg/day therapy after having been put under observation for a period of one week without medical treatment. There was an increase in the platelet count during the period of therapy culminating in a return to normal on the eighth day.

Case 2, who was in poor clinical condition at presentation, was treated with high-dose intravenous methylprednisolone (HIVMP) 30 mg/kg/day, resulting in the platelet count returning to a normal level (180,000/mm^3) on the second day of therapy.

HIVMP therapy is recommended in the treatment of life-threatening cases of thrombocytopenia because of its rapid action, limited side-effects, and its low cost.
Key words: thrombocytopenia, purpura, varicella, platelets, methylprednisolone.

Varicella is generally characterized by a mild viral infection with infrequent complications. Even though varicella associated thrombocytopenia is a rare entity, almost half of the cases of thrombocytopenia seen in combination with infections occur because of varicella[1]. Thrombocytopenia develops either when the rash appears or a few weeks later. However, it has also been reported during the incubation period. It has a sudden onset, with the platelet count usually falling below 20,000/mm^3. Spontaneous recovery usually occurs within a few weeks to a few months[2]. The clinical picture varies between mild transitory purpura and a fatal fulminant hemorrhage. The most dangerous complications are intracranial and intraparenchymal bleeding.

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There are different approaches regarding the treatment of this disease. This report describes two patients with varicella associated thrombocytopenia whose treatment protocols differed.

Case Reports

Case 1

A 4-year-7-month old girl was admitted with a three-day history of bruising on her body. She contracted varicella 12 days prior to admission. Physical examination revealed petechiae and ecchymoses scattered over the trunk and extremities. Crusts due to varicella were present. There was no evidence of mucosal bleeding, hepatosplenomegaly or lymphadenopathy. A complete blood count was normal except for a platelet count of 10,000/mm^3. Results of urinalysis were within normal limits. Bone marrow examination revealed hypercellularity with an increased number of megakaryocytes and no thrombocyte production. Platelet antibodies could not be documented because of technical reasons.

The patient was put under observation for one week without being given any therapy, but no increase in the platelet count (10,000/mm^3) was noted. Then prednisone therapy in a dose of 2 mg/kg/day was initiated. The platelet count rose to 40,000/mm^3 by the fourth day, and it reached 160,000/mm^3 by the eighth day. After two weeks of therapy, the dosage of prednisone was tapered off and then discontinued. Recovery was uneventful and the platelet count was found to be normal at subsequent follow-ups.

Case 2

An 8-year-old girl was admitted for evaluation of lethargy, fever, cough, easy bruising and bloody urine of three days' duration. Physical examination revealed a stuporous girl with ecchymoses and petechiae scattered all over her body.

Varicella crusts were present. There was a hematoma on each eyelid and nasal and oral bleeding were present. The urine was dark red in color. The heart rate was 100/min, blood pressure 100/60 mmHg, respiration rate 32/min and body temperature 38 °C. Crepitations were heard over the right lung. Hepatosplenomegaly and lymphadenopathy were absent.

Initial laboratory studies revealed a hemoglobin level of 10.9 g/dl, hematocrit 35%, While Blood Cell count 17,400/mm^3 with a predominance of neutrophils. The platelet count was 20,000/mm^3. Urinalysis revealed trace protein, numerous red cells, a few white cells and no casts. Chest x-ray revealed lobar pneumonia of the right lung. A bone marrow specimen showed abundant megakaryocytes with no thrombocyte production. Platelet antibodies could not be demonstrated because of technical reasons.

A few hours after admission the patient's condition worsened, and there was a deterioration in consciousness. Stiff neck with increased deep tendon reflexes and hyperpnea developed, clinically suggesting subarachnoidal hemorrhage. Lumbal puncture could not be accomplished because of bleeding at the puncture sites. Computed tomography could not be performed because of technical and economic reasons.

The patient was administered high-dose intravenous methylprednisolone (HIVMP) therapy in the following doses: 30 mg/kg/day for three days, followed by 20 mg/kg/day for four days. During the following four-week period decreasing doses of methylprednisolone of 10 mg/kg/day, 5 mg/kg/day, 2 mg/kg/day and 1 mg/kg/day were administered each for one week, respectively. The patient also received penicillin and gentamicin to treat her pneumonia. Although the occurrence of viral pneumonia is always a possible complication in varicella, the patient's fever and leukocytosis with a predominance of neutrophils, suggested a bacterial origin of the disease. The platelet count rose to 180,000/mm^3, on the second day of therapy and her state of consciousness improved. The ecchymoses gradually faded and the hematuria disappeared. During the course of therapy, the platelet count remained above 150,000/mm^3 and only once, when the dose was reduced to 5 mg/kg/day, did it fall to 50,000/mm^3, but rapidly returned to normal levels. The pneumonia was no longer present. Side-effects encountered during therapy were weight gain of two kilograms and slight blood pressure elevations which responded well to therapy. There was no fall in the platelet count after the cessation of therapy.

Discussion

Different methods of therapy are suggested when treating infection associated thrombocytopenia such as clinical observation along with supportive therapy, oral prednisone therapy (2 mg/kg/day), high-dose intravenous methylprednisolone therapy, intravenous gamma globulin therapy and splenectomy. The platelet count generally returns to normal levels within two weeks even without therapy[3]. Intravenous gamma globulin causes a rapid increase in the platelet count[4]. This treatment which is costly in Turkey, is associated with such side-effects as hemolysis and ABO alloimmunization. Platelet transfusion has no beneficial effect because transfused platelets are rapidly destroyed by antibodies[1]. The use of steroids in treating varicella infection is controversial because it can lead to a spread of infection, increase in mortality, hemorrhagic rash, and a deterioration of the microscopic pathology of uncomplicated varicella[5]. On the other hand, corticosteroids increase the platelet count by causing immunosuppression, decreasing platelet antibody production, causing a hemostatic effect on the vessel wall and inhibiting phagocytosis in the accessory cell system[6,7]. Steroids have been used in varicella associated thrombocytopenia. They can only have an

effect on immune-mediated thrombocytopenia, but do not influence direct thrombocyte-virus interaction[2,7].

Recent reports in the literature indicate that the platelet count returns to normal within three days in patients with idiopathic thrombocytopenic purpura who are treated with high-dose intravenous methylprednisolone (HIVMP)[8,9]. Since this treatment is relatively less costly than gamma globulin therapy, and yields comparably good results, it is emphasized that it be the treatment of choice in the management of patients with idiopathic thrombocytopenic purpura. It is also stressed that clinical observation without medical therapy have particularly no difference in their effect on increasing the platelet count[8,9]. We had to resort to the use of corticosteroids because the first patient had varicella for a period of 12 days, while the second patient was suffering from the illness for 15 days. Case 1 was in good clinical condition at presentation. She had no mucosal bleeding, and therefore, was put under observation without any medical therapy for one week. However, no increase in platelet count was noted. It was then decided that prednisone 2 mg/kg/day be administered and her platelet count returned to normal within a period of eight days of therapy.

We previously administered HIVMP to a patient with thrombocytopenia caused by an innoculation with the Measles-Mumps-Rubella vaccine who made a rapid recovery after treatment[10].

On the other hand, Case 2 was in poor clinical condition at presentation. She had impaired consciousness and active mucosal hemorrhaging. We therefore, decided to treat her with HIVMP and we observed with satisfaction that the platelet count rapidly increased.

After our experience with these two cases, we are of the opinion that when a life-threatening hemorrhage is present in patients afflicted with thrombocytopenia, HIVMP therapy is the treatment of choice. Moreover, this therapy has the advantage of being relatively inexpensive, gives prompt results, and is associated with few side-effects.

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